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10/033,308	10/24/2001	M. Parameswara Reddy	2058-181	8198

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PATENT LEGAL DEPARTMENT/A-42-C
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EXAMINER	
EPPERSON, JON D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/033,308	REDDY ET AL.	
	Examiner	Art Unit	
	Jon D Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,18 and 20-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,18 and 20-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *11/10/03*.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. The Response filed June 30, 2004 is acknowledged.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of the Claims

3. Claims 1-15, 18, and 20-29 were pending. Applicants added claims 30-36 and amended claims 1, 12, 20, 26 and 27. Therefore, 1-15, 18, 20-36 are currently pending.

Withdrawn Objections/Rejections

4. All outstanding rejections and/or objections are withdrawn in view of Applicants' arguments and/or amendments.

New Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-4, 9-11, 18, 20-21, 25-31, 33 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hearn (Hearn, M. T. W. 1,1'-Carbonyldiimidazole-Mediated Immobilization of Enzymes and Affinity Ligands in "Methods in Enzymology" Ed. Mosbach, K. New York: Academic Press, Inc. **1987**, Vol. 135, pages 102-117) and Stolowitz et al. (WO 87/06586) (of record).

For ***claims 1, 20, 26-31 and 33***, Hearn (see entire document) discloses the use of a coupling agent, 1,1-carbonyldiimidazole (CDI), to immobilize "macromolecules" including proteins on a solid support for use in affinity chromatography, which reads on claim 1 (e.g., see Introduction). For example, Hearn discloses **(a)** reacting an available hydroxyl group on a solid support with an activating L_1-X-L_2 compound wherein the L_1 is displaced (e.g., see schematic diagrams bridging pages 105-106 wherein Hearn discloses the use of CDI

having two azole rings and a carbonyl group that represents L_1/L_2 and X, respectively; see also the "Activation" step on page 105 wherein the L_1 azole ring is displaced). In addition, Hearn discloses **(b)** providing a biological molecule having at least one reactive amino ... group (e.g., see page 106, schematic on top of page, "Coupling" step wherein R-NH_2 is added). Hearn also discloses the use of a macromolecule selected from the group consisting of nucleic acids, polypeptide chains and carbohydrates (e.g., see Hearn, page 102, last paragraph, "The ligand, frequently itself a protein, must be chemically coupled either directly to a suitably activated insoluble, inert matrix ... or coupled via a leash or spacer group"; see also page 112, Table IV; see also). Finally, Hearn discloses **(c)** reacting the biological molecule with the activated support, thereby displacing L_2 and covalently attaching the biological molecule to the solid support (e.g., see Hearn, page 106, "Coupling" step wherein the R_2 azole ring is displaced and the R-NH_2 is covalently attached to the solid support). In addition, Hearn also disclose a material selected from the group consisting of cellulose, agarose, polypropylene, polystyrene, polymethacrylate, and nylon as disclosed in claims 20 and 27 and "organic polymers" disclosed in claim 26 (e.g., see paragraph bridging pages 108-109 wherein, for example, agarose, cellulose, Fractogel, Tyropearl are disclosed). Furthermore, Hearn disclose the use of biological molecules selected from the group consisting of hormones, therapeutic drugs and drugs of abuse as disclosed in claim 29 (e.g., page 112, Table IV). Finally, Hearn also disclose the use of "organic polymers", L_1/L_2 selected from the group "consisting of ... imidazole, triazole" as disclosed by claim 30 (e.g., see abstract wherein CDI is disclosed; see also page 106,

paragraph 1 wherein "triazole" is disclosed; see also page 108-109 wherein various polymers are disclosed).

For ***claim 2***, Hearn discloses, for example, "imidazole" rings (e.g., see abstract wherein CDI is disclosed; see also page 106, paragraph 1 wherein "triazole" is disclosed).

For ***claim 3***, Hearn discloses, for example, -C(=O)- (e.g., see abstract wherein CDI contains the requisite carbonyl).

For ***claim 4 and 31***, Hearn discloses, for example, 1,2,4-carbonyl di-triazole (e.g., see page 106, paragraph 1; see also page 107, Table I).

For ***claim 9***, Hearn discloses organic solutions including acetone and dioxane (e.g., see page 107, Table I).

For ***claim 10***, Hearn discloses, for example, triethylamine (e.g., see page 110, paragraph 1).

For ***claim 11***, Hearn discloses, for example, coupling the activated matrix in aqueous buffer (e.g., see page 106, last paragraph, "Because protein coupling reactions are generally carried out in an aqueous milieu ...").

For ***claims 18 and 21***, Hearn discloses a "washing" step (e.g., see page 108, second to last paragraph, "The activated gel should be washed with fresh anhydrous dioxane or acetone to remove the liberated imidazole").

For ***claims 25 and 34***, Hearn discloses polynucleotides (e.g., see page 110, first full paragraph, "The reaction of N-nucleophiles ... such as ... amino acids, peptides, proteins and polynucleotides ... with CDI activated matrices").

The prior art teachings of Hearn differ from the claimed invention as follows:

For ***claim 1***, Hearn is deficient in that the reference does not specifically teach the use of an "available amino group on the solid support" to react with the L_1-X-L_2 activating agent. Hearn only teaches the use of an available "hydroxyl" group (e.g., see page 105, schematic at bottom of page, "Activation" step wherein the –OH reacts with the CDI), which results in a "carbamate" [i.e., RO-C(=O)-NHR'] as opposed to the requisite "urea" linkage [i.e., RNH-C(=O)-NHR'].

However, Stolowitz et al. teach the following limitations that are deficient in Hearn:

For ***claim 1***, Stolowitz et al. teach the use of CDI for the immobilization of biological ligands used in affinity chromatography with an "available amino group on the solid support" (e.g., see abstract, "The invention relates to the functionalization of particulate bonded phase chromatographic supports prepared by silanization of silica gel or controlled pore glass and containing pendant primary alkyl amine groups. Functionalization results from the activation of the amines by reaction with N,N'-carbonyldiimidazole (CDI), or a related azolide, in anhydrous organic solvent, followed by derivatization of the support. Derivatization results from reaction of the activated support with a functionalizing reagent consisting of a primary or secondary, alkyl or aryl amine in organic solvent, or from an aqueous solution of the amine or its salt. A urea linkage results through which the functionalizing reagent is covalently attached to the support"; see also page 9, formula 7 wherein the urea linkage is shown; see also Summary of Invention, "In addition, a number of important specific objectives are also achieved using the present invention, including: The use of N,N'-carbonyldiimidazole for

the activation of a chromatographic support with other than pendant hydroxyl groups; The preparation of a urea derivative of a bonded phase chromatographic support and the unique hydrophilic nature of the urea linkage"; see also Example 1, lines 8-18; see also page 3, lines 14-20; see also page 3, lines 21-26).

It would have been obvious to one skilled in the art at the time the invention was made to immobilize "macromolecule" ligands as taught by Hearn with CDI using "free amino groups" as taught by Stolowitz et al. instead of "free hydroxyl groups" as taught by Hearn because Stolowitz et al. explicitly state that "free amino groups" can be used for the same purpose i.e., immobilization of ligands that are used in affinity chromatography (e.g., see Stolowitz et al., abstract). Furthermore, one of ordinary skill in the art would have been motivated to use the "free amino groups" because Stolowitz et al. explicitly state that they obtain "near quantitative derivatization of bonded supports ... by this synthetic route" (e.g., see Stolowitz et al., page 4, lines 29-30). Stolowitz et al. also state that their method is "versatile" because "almost [an] infinite variety of ligands ... can be employed as functionalizing reagents" (e.g., see Stolowitz et al., page 4, lines 34-35) and their method allows for "[t]he use of N,N'-carbonyldiimidazole for the activation of a chromatographic support with other than pendant hydroxyl groups" (e.g., see Stolowitz et al., page 4, lines 23-25). In addition, Stolowitz et al. state that their method provides for a physical barrier that enhances the efficiency of the chromatographic procedures (e.g., see Stolowitz et al., page 4, lines 11-19, "The preparation of a physical barrier preventing interaction between surface silanols and sample components; The derivatization of the physical barrier preventing interaction between the hydrophobic silane backbone and

sample components; and the functionalization of the physical barrier to impart properties resulting in selective retention of sample components." Stolowitz et al. also state that the "urea" linkage has favorable properties (e.g., see Stolowitz et al., page, 7, first full paragraph, "The urea linkage ... is uncharged under normal chromatographic conditions and provides a hydrophilic barrier masking the properties of the silane backbone and the residual silanol activity beneath it"). Furthermore, one of ordinary skill in the art would have reasonably expected to be successful because both Hearn and Stolowitz et al. use the same coupling reagents (e.g., CDI) with the same solid supports (e.g., see Hearn, page 109, paragraph 1 wherein porous silicas, controlled pore glasses are disclosed; see also Stolowitz et al., "Summary of Invention" wherein controlled pore glasses and porous silicas are also disclosed) for the same purpose (i.e., affinity chromatography). Stolowitz et al. also state that in addition to the short "di-glycine" peptide (e.g., see Stolowitz et al. page 9, lines 2-4) disclosed as a functional ligand, "almost [an] infinite variety of ligands ... can be employed as functionalizing reagents" (e.g., see Stolowitz et al., page 4, lines 34-35), which would include the "larger" peptide/protein "macromolecules" disclosed by Hearn.

Response to Arguments

7. To the extent that Applicants' arguments directed toward the previous 35 USC § 102(b) rejection under Stolowitz et al. (e.g., see 6/30/04 Response, page 11, paragraph 1) can be applied to the present 35 USC § 103(a) rejection under Stolowitz et al. and Hearn, the following comments are noted.

Applicants argue that Stolowitz et al. does not teach a "biological macromolecule" (e.g., see 6/30/04 Response, page 11, paragraph 1).

This is not found persuasive for the following reasons:

The Examiner contends that the combined teachings of Stolowitz et al. and Hearn teach biological macromolecules (e.g., see page 110, first full paragraph, "The reaction of N-nucleophiles ... such as ... amino acids, peptides, proteins and polynucleotides ... with CDI activated matrices").

8. Claims 1-15, 18, 20-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hearn (Hearn, M. T. W. 1,1'-Carbonyldiimidazole-Mediated Immobilization of Enzymes and Affinity Ligands in "Methods in Enzymology" Ed. Mosbach, K. New York: Academic Press, Inc. **1987**, Vol. 135, pages 102-117) and Stolowitz et al. (WO 87/06586) (of record) and Milton (US 6,146,833; of record) and Okamoto et al. (US 6,476,215) and Guo et al. (Nuc. Acids Res. 1994, pp. 5456-5465).

For ***claims 1-4, 9-11, 18, 20-21, 25-31, 33 and 34***, the combined teachings of Hearn and Stolowitz et al. disclose all the limitations stated in the 35 U.S.C. 103(a) rejection above (incorporated in its entirety herein by reference), which renders obvious claims 1-4, 9-11, 18, 20-21, 25-31, 33 and 34.

The prior art combined teachings of Hearn and Stolowitz et al. differ from the claimed invention as follows:

For ***claims 5-6, 22-23, 35-36***, the prior art teachings of Hearn and Stolowitz et al. differ from the claimed invention by not reciting the deposition of compounds in a particular area on the support (i.e. using printing).

For ***claims 7-8, 24***, the prior art teachings of Hearn and Stolowitz et al. differ from the claimed invention by not reciting the use of a humid chamber.

For ***claims 12-15, 32***, the prior art combined teachings of Hearn and Stolowitz et al. differ from the claimed invention by not reciting the use of a plate or film.

However, the combined teachings of Milton et al. Okamoto et al. and Guo et al. teach the following limitations that are deficient in the combined teachings of Hearn and Stolowitz et al.:

For ***claims 5-6, 22-23, 35-36***, However, the use of printing techniques to deposit biological compounds onto solid supports was well established in the art at the time of filing, as evidenced by the teachings of Milton, Okamoto et al. and Guo et al. (e.g., see for example, column 12, lines 24-41; see also column 8, line 33; see also column 11, line 62; see also column 17, line 2; see also Guo et al., page 5457, 1st column; see also Okamoto et al., columns 1-3). The reference teaches methods for printing compounds to make an array. See Examples 5 and 6 wherein spot diameter is, for example, 250 μm (note this procedure is *referred to in the instant specification,* pages 9 and 10). Milton specifically teaches the immobilization of e.g. oligonucleotides and peptides, see Examples 3-9 of the reference.

For ***claims 7-8 and 24***, the combined teachings of Milton, Okamoto et al. and Guo et al further teach a humid chamber during the attachment of the probes to their arrays (e.g.,

see Guo, page 5457, 1st column; see also Okamoto et al., column 18, lines 42-46). This step is used to complete the reaction and/or to incubate the arrays.

For ***claims 12-15, 32***, the combined teachings of Milton, Okamoto et al. and Guo et al. further teaches the use of a plate and a film (e.g., see figures 1-7; see also column 2, lines 5-8 wherein glass slides, polymer films, silicon wafers are disclosed; see also column 2, lines 47-50; see also column 3, line 4; see especially claim 23, "the solid support provided is a film"). In addition, Milton teaches polypropylene, which is an organic polymer (e.g., see column 2, line 5; see also figures 1, 6, 10, 14; see also Examples; see also claims 2, 4, 8 and 11).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use the CDI immobilization chemistry taught by Hearn and Stolowitz et al. in an array-type format using a "printing method" to deliver the amine compound (e.g. oligonucleotides or peptides) as taught by Milton, Guo and Okamoto because "immobilization" of biomolecules is required in each case (i.e., the references represent analogous art). One of ordinary skill would have been motivated to do so due in order to create covalently attached amine bound biomolecules "immobilized at site specific locations" as taught by Milton (for example). In addition, Stolowitz et al. and Hearn disclose that the use of CDI would provide near "quantitative" yields for "immobilization" of biomolecules as required by Milton including polypeptides, proteins and nucleic acids (e.g., see Stolowitz et al., page 4, lines 29-30, "The near quantitative derivatization of bonded supports obtained by this synthetic route [i.e., CDI with amine]"). In addition, a person of skill in the art would have been motivated to use a "humid chamber" to complete

the reaction and/or to incubate the arrays once created. One of ordinary skill would have had a high expectation of success as these printing techniques were well established in the art at the time of filing especially on glass substrates that can withstand harsh conditions (e.g., see Milton, column 2, lines 5-10; see also Okamoto et al., column 6, lines 31, 38, 67; see also figures 1-2; see also column 12, line 53; see also Guo, Title and abstract) and the methods of immobilization include the same coupling reagent e.g., CDI.

Response to Arguments

9. To the extent that Applicants' arguments directed toward the previous 35 USC § 103(a) rejections under Stolowitz et al., Milton, Guo et al. and Okamoto et al. (e.g., see 6/30/04 Response, page 11, paragraph 1) can be applied to the present 35 USC § 103(a) rejection under Hearn, Stolowitz et al., Milton, Guo et al. and Okamoto et al., the following comments are noted.

[1] Applicants argue, "Stolowitz et al. teaches separation of the claimed biological molecules, and expressly teaches against covalent attachment of the claimed biological molecules" (e.g., see 6/30/04 Response, page 12, last paragraph; see also page 18, first full paragraph).

[2] Applicants argue, "The proposed combination of Stolowitz et al. and Milton is completely contrary to the teachings of Stolowitz et al. If Stolowitz et al. is combined with Milton, Stolowitz et al. would not work for its intended purpose. No person of ordinary skill in the art would make the combination" (e.g., see 6/30/04 Response, paragraph bridging pages 12-13, see also page 15, paragraph 3).

[3] Applicants argue that Stolowitz et al. "expressly teaches no irreversible absorption i.e., covalent attachment of these [biological macromolecules]" (e.g., see 6/30/04 Response, bottom of page 13).

[4] Applicants argue that Milton does not provide the requisite motivation to modify or combine the references to arrive at Applicants' claimed invention and further state that Milton discloses immobilizing biopolymers with "entirely different" attachment chemistry than the attachment chemistry claimed by Applicants (e.g., see 6/30/04 Response, paragraph bridging pages 13-14; see also page 15, paragraph 2).

[5] Applicants argue that the combined references don't teach "a plate or a film" or a solid support consisting of "cellulose, agarose ... [etc.]" or "providing a solid support comprised of an organic polymer having at least on amino group" (e.g., see 6/30/04 Response, bottom of page 14).

[6] Applicants argue, "Milton does not teach or suggest: (1) amine derivatized plates ... (3) amine derivatized organic polymers" (e.g., see 6/30/04 Response, paragraph bridging pages 14-15).

[7] Applicants argue, that there is no description in Okamoto et al., Guo et al., Milton, Elkins et al. of (i) 'reacting the available amino group on the solid support with an activating compound' of Applicants claimed formula 'L1-X-L2' ..." (e.g., see 6/30/04 Response, page 16, first full paragraph; see also bottom of page 17).

[8] Applicants argue, "one of ordinary skill in the art would not be motivated to modify or combine Stolowitz et al., and Milton, and Okamoto et al. and Guo et al ... (i) Neither Okamoto et al. alone or in combination suggests covalent attachment of biological macromolecules to a

solid support using Applicants' claimed compounds; (ii) ... There is no suggestion in Milton of solid supports 'having at least one amino group' ... (iii) Stolowitz directly teaches against covalently attaching biological macromolecules" (e.g., see 6/30/04 Response, bottom of page 16).

This is not found persuasive for the following reasons:

[1] The Examiner respectfully disagrees. Stolowitz et al. state that "almost infinite variety of ligands which can be employed as functionalizing reagents" (e.g., see Stolowitz et al., page 4, lines 34-35), which would include "biological macromolecules" and thus does not represent a "teaching away" as Applicants claim. In addition, Hearn explicitly states (see 35 USC § 103(a) rejection above) that "biological macromolecules" can be immobilized for "separation" techniques thus rendering Applicants' arguments moot (e.g., see page 110, first full paragraph, "The reaction of N-nucleophiles ... such as ... amino acids, peptides, proteins and polynucleotides ... with CDI activated matrices").

[2] Applicant's arguments fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references. Here, Applicants never state how or why Stolowitz et al. would "not work" for its intended purpose. In addition, Applicants never address the issue of whether or not Milton would work when combined with Stolowitz et al. The Examiner contends that both would work.

[3] The Examiner respectfully contends that Applicants are factually mistaken. Stolowitz et al. do not teach that the ligand cannot be irreversibly bound to the solid-support as Applicants contend, rather Stolowitz et al. teach that the protein macromolecule to which the ligand binds

during separation cannot be covalently bound. Stolowitz et al. state that "almost infinite variety of ligands which can be employed as functionalizing reagents [i.e., covalently bound]" (e.g., see Stolowitz et al., page 4, lines 34-35), which would include "biological macromolecules" and thus does not represent a "teaching away" as Applicants contend. In addition, Hearn explicitly states (see 35 USC § 103(a) rejection above) that "biological macromolecules" can be immobilized for "separation" techniques thus rendering Applicants' arguments moot (e.g., see page 110, first full paragraph, "The reaction of N-nucleophiles ... such as ... amino acids, peptides, proteins and polynucleotides ... with CDI activated matrices").

[4] First, the Examiner respectfully contends that Applicants are factually mistaken. Both Milton and Stolowitz et al. [and now Hearn] disclose immobilizing ligands on glass substrates using, for example, carbodiimides, which is not "entirely different" attachment chemistry (e.g., see Milton, "Additionally ... oligonucleotides have been immobilized by covalently attaching activated oligonucleotides to the solid support ... with, e.g., a carbodiimide"). Second, In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, one of ordinary skill would have been motivated to do so due in order to create covalently attached amine bound biomolecules "immobilized at site specific locations" as taught by Milton (for example). In addition, the combined teachings of Stolowitz et al. and

Hearn disclose that the use of CDI would provide near "quantitative" yields for "immobilization" of biomolecules including polypeptides, proteins and nucleic acids (e.g., see Stolowitz et al., page 4, lines 29-30, "The near quantitative derivatization of bonded supports obtained by this synthetic route [i.e., CDI with amine]").

In addition, the Examiner contends that this interpretation of Milton is too narrow and further fails to appreciate the teachings of Okamoto et al. and Guo et al. For example, Milton states, "Derivatized polypropylene films, glass slides and silicon wafers have been used for the solid support synthesis of oligonucleotides and peptides at site specific locations on the film, slide or wafer. These materials have been fairly successful because the glass, polypropylene and silicon withstand the physical and chemical rigors of the synthesis and hybridization processes" (e.g., see Milton, column 2, lines 5-10). Thus, Applicants narrow assessment of Milton et al. is unwarranted because Milton et al. explicitly states "oligonucloetides and peptides [can successfully be deposited] at site specific locations on the film, slide or wafer" (e.g., see Milton, column 2, lines 7-8), which would encompass the glass substrates disclosed by Stolowitz et al. In addition, both Okamoto et al. and Guo et al. teach that glass substrates can be used (e.g., see Okamoto et al., column 6, lines 31, 38, 67; see also figures 1-2; see also column 12, line 53; see also Guo, Title and abstract).

[5] The Examiner contends that the new rejection above explicitly addresses each of the identified limitations with a specific citation therein. Here, the limitations to which Applicants refer (e.g., plates and films in claim 12, polypropylene in claims 20 and 27, and organic polymer in claim 26) are taught by the combined references (see newly amended rejection above).

[6] In response to applicant's arguments against the Milton reference individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

[7] In response to applicant's arguments against the Okamoto et al./ Guo et al. references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

[8] The Examiner contends (i) "there is no requirement that the prior art provide the same reason as the applicant to make the claimed invention", see MPEP § 2144"), (ii) in response to applicant's arguments against the Milton reference individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986) and (iii) Stolowitz does not "teach against" covalently attaching biological molecules (e.g., see section **[3]** above).

Conclusion

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
September 12, 2004

PRIMARY EXAMINER